[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Derivatives of the Aldehydrol Form of Sugars. V.[1] Rotatory Power

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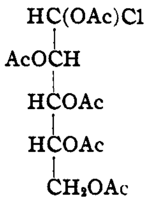
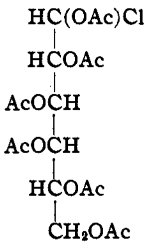
In a previous publication,[3] it was shown that the *aldehydo*-sugar acetates add one mole of an acyl halide to form predominantly one of the two isomers predictable on stereochemical grounds. A method for obtaining the second form was then obtained[1] when it was found that a mixture of the two isomers was produced on treatment with zinc chloride, an interconversion procedure established by Hudson and co-workers[4] for the α,β or anomeric[5] forms of 1-chloro-1-methoxy-*aldehydo-d*-arabinose tetraacetate. We have now extended this work in the galactose and arabinose structures and have obtained, in a state of optical purity, the α,β-forms of the acetyl chloride and acetyl bromide carbonyl addition compounds of *aldehydo-d*-galactose pentaacetate and of *aldehydo-d*-arabinose tetraacetate. The application of the terms α and β, as suggested by Dimler and Link,[6] is based upon the usage proposed by Hudson[7] for the cyclic structures, in which that derivative, in the *d*-series, having the more positive rotation, is assigned the prefix α.

The optical rotation measurements on these four anomeric pairs in two sugar structures are tabulated in Table I. We have applied to the recorded rotations the isorotation rules of Hudson,[7] according to which the rotation contribution of carbon one is designated as $+A_{Cl}$ for the α-form and $-A_{Cl}$ for the β-form. The rotation contribution of the remaining asymmetric centers is designated as $+B$. The A and B values may then readily be calculated.



$$\begin{array}{c}\mathrm{HC(OAc)Cl}\\ |\\ \mathrm{AcOCH}\\ |\\ \mathrm{HCOAc}\\ |\\ \mathrm{HCOAc}\\ |\\ \mathrm{CH_2OAc}\end{array}$$

1-Chloro-*aldehydo-d*-arabinose pentaacetate



$$\begin{array}{c}\mathrm{HC(OAc)Cl}\\ |\\ \mathrm{HCOAc}\\ |\\ \mathrm{AcOCH}\\ |\\ \mathrm{AcOCH}\\ |\\ \mathrm{HCOAc}\\ |\\ \mathrm{CH_2OAc}\end{array}$$

1-Chloro-*aldehydo-d*-galactose hexaacetate

It is seen from Table I that the isorotation rules of Hudson apply to these compounds with a high degree of exactitude. Thus, the value of the stem B remains nearly constant in the same sugar structure when the nature of the halogen is changed. The values of A_{Br} and of A_{Cl} are very nearly constant for each of the two sugars measured. The quantity $A_{Br}-A_{Cl}$ was found to be 20,600. This compares favorably with the average value of 21,400 recorded by Hudson[8] and by Brauns[9] for the cyclic acetohalogen sugars.

In addition to the six anomeric acyclic forms listed in Table I, eight more pairs are tabulated by Wolfrom, Konigsberg and Moody.[10] To these may be added the anomeric forms of 1-thioethoxy-*aldehydo-d*-glucose hexaacetate.[11] If we omit from this list those α,β-pairs in which the rotation of both members is known with precision to only one significant figure (specific rotation less than 10°), we then have a number of anomeric pairs as listed in Table II. The application of the isorotation rules of Hudson to this group of compounds is shown in Table II. The values of B in the arabinose series vary from 12,000 to 15,000 through four different types of substituent groups on carbon one. The A_{OMe} value of 1600 in the arabinose structure compares with that of 2800 for mannose. This is a large percentage difference but in absolute value, it is well within the usual range of agreement considered satisfactory for the cyclic structures.

The data of Table I also exhibit interesting melting point regularities. Thus in the *d*-galactose structure, the α-form is consistently the lower melting, whereas the reverse holds for the *d*-arabinose structure. The higher melting form, in both sugars, was the one obtained[3,12] directly from the acyl halide when the zinc chloride catalyst was omitted. The higher melting form was also

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[1] Previous publication in this series: M. L. Wolfrom and R. L. Brown, THIS JOURNAL, **63**, 1246 (1941).

[2] Du Pont Fellow, 1941–1942.

[3] M. L. Wolfrom, *ibid.*, **57**, 2498 (1935).

[4] Edna M. Montgomery, R. M. Hann and C. S. Hudson, *ibid.*, **59**, 1124 (1937).

[5] C. N. Riiber and N. A. Sørensen, *Kgl. Norske Videnskab. Selskabs, Skrifter* 1933, No. 7, p. 9; *Chem. Zentr.*, **105**, I, 2738 (1934).

[6] R. J. Dimler and K. P. Link, THIS JOURNAL, **62**, 1216 (1940).

[7] C. S. Hudson, *ibid.*, **31**, 66 (1909).

[8] C. S. Hudson, Scientific Paper of the Bureau of Standards No. 533, Government Printing Office, Washington, D. C., 1926, p. 313.

[9] D. H. Brauns, *Bur. Standards J. Research*, **7**, 574 (1931).

[10] M. L. Wolfrom, M. Konigsberg and F. B. Moody, THIS JOURNAL, **62**, 2343 (1940).

[11] M. L. Wolfrom, D. I. Weisblat and A. R. Hanze, *ibid.*, **62**, 3246 (1940).

[12] M. L. Wolfrom and M. Konigsberg, *ibid.*, **60**, 288 (1938).

Table I

Rotatory Relationships

Compound	Isomer	Ratio,[b] %	M. p., °C.	$[\alpha]^{25}_D$, abs. $CHCl_3$	$[M]_D$	B	A_{Br}	A_{Cl}	$A_{Br} - A_{Cl}$
1-Chloro-*aldehydo-d*-galactose	α[1]	76[1]	153–154	+62°	+29,000	4,200		24,800	20,600
hexaacetate	β[3]	24[1]	174–175	−44	−20,600				
1-Bromo-*aldehydo-d*-galactose	α[a]	74	142.5–143	+98	+50,300	4,900	45,400		
hexaacetate	β[12]	26	179–181	−79	−40,500				
1-Chloro-*aldehydo-d*-arabinose	α[a]	31	109–110	+97	+38,500	13,400		25,100	20,600
pentaacetate	β[a]	69	67.5–68.5	−29.5	−11,700				
1-Bromo-*aldehydo-d*-arabinose	α[a]	32	129–130	+136	+60,000	14,300	45,700		
pentaacetate	β[a]	68	63–64	−71	−31,300				

[a] This work. [b] First two values were calculated on the basis of reaction equilibrium rotations; other values on the basis of the rotation of the crude mixture isolated in high yield (80–90%).

Table II

Rotatory Relationships

Compound	Isomer	M. p., ° C.	$[\alpha]^{20-25}_D$, abs. $CHCl_3$	$[M]_D$	B	$A_{(OMe)}$
1-Chloro-*aldehydo-d*-arabinose	α[a]	109–110	+97°	+38,500	13,400	
pentaacetate	β[a]	67.5–68.5	−29.5	−11,700		
1-Bromo-*aldehydo-d*-arabinose	α[a]	129–130	+136	+60,000	14,300	
pentaacetate	β[a]	63–64	−71	−31,300		
1-Chloro-1-methoxy-*aldehydo-d*-	α[4]	73	+52.5	+19,400	15,000	
arabinose tetraacetate	β[4]	71	+29	+10,700		
1-Methoxy-*aldehydo-d*-arabinose	α[4]	68–70	+35	+13,700	12,100	1,600
pentaacetate	β[4]	76	+27	+10,600		
1-Methoxy-*aldehydo-l*-arabinose	α[10]	67–68	−34	−13,300	−12,000	−1,400
pentaacetate	β[10]	76–77	−27	−10,600		
1-Methoxy-*aldehydo-d*-mannose	α[10]	84–85	+23	+10,700		2,800
pentaacetate	β[10]	95.5–96	+11	+5,100		

[a] This work.

the minor constituent of the zinc chloride equilibrium mixture. The general stability of these acyclic acetohalogen sugars is greater than that of their cyclic analogs. With the exception of a few unstable levorotatory (*d*-series) acetochloro (and one acetobromo) compounds,[13] the cyclic acetohalogen sugars are known only in their dextrorotatory (*d*-series) forms.

Experimental

α- and β-1-Chloro-*aldehydo-d*-arabinose Pentaacetates.—To a solution of 10 g. of *aldehydo-d*-arabinose tetraacetate[14] in 100 cc. of acetyl chloride was added 4 cc. of a 10% solution of freshly fused zinc chloride in glacial acetic acid (containing a few drops of acetic anhydride). After standing for thirty-six hours at room temperature (20–25°), the solution was poured into two liters of ice and water. The acidic liquors were decanted from the precipitated sirup and fresh ice-water added. The sirup crystallized after standing at 5° for a day. The crude product was removed by filtration, washed with cold water and air-dried on the filter and then at room temperature and under reduced pressure over phosphorus pentoxide; yield 10 g. (80%), m. p. 63–75°; spec. rot. +10° (25°, *c* 1.5, abs. $CHCl_3$, D line).

The crude product (9.5 g.) was dissolved in 7 parts of hot absolute ethanol and cooled to 5°. Three grams of crystalline material was removed by filtration; m. p. 91–100°, spec. rot. +55.5° ($CHCl_3$). The filtrate was concentrated to 40 cc. under reduced pressure and cooled to 0°. The precipitated crystalline material was removed by filtration yield 4.1 g., m. p. 66–68°, spec. rot. −23° ($CHCl_3$). An additional 0.5 g. was obtained by evaporation of the mother liquors to 5 cc.

The dextrorotatory fraction was recrystallized four times from four parts of anhydrous ethanol to yield 1.4 g. of pure α-1-chloro-*aldehydo-d*-arabinose pentaacetate; m. p. 109–110°, spec. rot. +97.1° (20°, *c* 1.3, abs. $CHCl_3$, D line). For the enantiomorph, Wolfrom and Konigsberg[12] recorded the constants: m. p. 109–110°, spec. rot. −96° (25°, abs. $CHCl_3$, D line).

The levorotatory fraction was recrystallized once from 3 parts of absolute ethanol, once from 4 parts of 3:1 petroleum ether–ethanol, and twice from 100 parts of 2:1 ether–petroleum ether to yield 2 g. of pure β-1-chloro-*aldehydo-d*-

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(13) E. Fischer and E. F. Armstrong, *Ber.*, **34**, 2885 (1901); C. S. Hudson and J. M. Johnson. This Journal, **38**, 1223 (1916); H. H. Schlubach. *Ber.*, **59B**, 840 (1926); H. H. Schlubach, P. Stadler and Irene Wolf, *ibid.*, **61B**, 287 (1928); H. H. Schlubach and R. Gilbert. *ibid.*, **63B**, 2292 (1930); H. H. Schlubach and E. Wagenitz, *Z. physiol. Chem.*, **213**, 87 (1932).

(14) M. L. Wolfrom, D. I. Weisblat. W. H. Zophy and S. W. Waisbrot. This Journal, **63**, 201 (1941).

arabinose pentaacetate; m. p. 67.5–68.5°; spec. rot. −29.5° (26°, *c* 1.3, abs. $CHCl_3$, D line).

The α-isomer was soluble in chloroform and acetone, moderately soluble in ethanol, methanol and benzene, slightly soluble in ether and was insoluble in petroleum ether (30–60°) and water. The β-isomer was generally more soluble than its α-counterpart.

Anal. Calcd. for $C_5H_6O_5(CH_3CO)_5Cl$: Cl, 8.94; saponification value (6 equivs.), 15.12 cc. 0.1 *N* NaOH per 100 mg. Found for α-isomer: Cl, 8.89; saponification value, 15.12 cc. Found for β-isomer: Cl, 9.06; saponification value. 15.11 cc.

α- and β-1-Bromo-*aldehydo-d*-arabinose Pentaacetates.—A solution of 15 g. of *aldehydo-d*-arabinose tetraacetate in 100 g. (67 cc.) of acetyl bromide was treated with 4 cc. of the interconverting reagent under the same conditions as described previously for the synthesis of the α- and β-1-chloro-*aldehydo-d*-arabinose tetraacetates and the product isolated in the same manner; yield 17 g. (81%), m. p. 60–100°, spec. rot. −5.1° (20°, *c* 3.4, abs. $CHCl_3$, D line).

The crude product was dissolved in hot acetone (20 cc.) and allowed to cool to room temperature. The crystalline material (4.3 g.) was removed by filtration; m. p. 125–127°, spec. rot. +127° ($CHCl_3$). The filtrate was evaporated to dryness in a stream of dry air to yield a sirup which was dissolved in warm ether–petroleum ether (30–60°) and allowed to cool to room temperature. Five grams of crystalline material was separated by filtration; m. p. 61–67°, spec. rot. −46.5° ($CHCl_3$). An additional 5 g. of material was obtained when the mother liquors were worked up in the same manner; m. p. 62–70°, spec. rot. −56° ($CHCl_3$).

The dextrorotatory fraction (4.3 g.) was crystallized four times from moderately large volumes of acetone–ether–petroleum ether and finally from ether to yield 1 g. of pure α-1-bromo-*aldehydo-d*-arabinose pentaacetate; m. p. 129–130°, spec. rot. +135.7° (25°, *c* 3, abs. $CHCl_3$, D line). For the enantiomorph, Wolfrom and Konigsberg[15] recorded the constants: m. p. 130–131°, spec. rot. −134° (25°, abs. $CHCl_3$, D line).

The combined levorotatory fractions (10 g.) were carefully crystallized seven times from dry ether to yield 3 g. of pure β-1-bromo-*aldehydo-d*-arabinose pentaacetate; m. p. 63–64°, spec. rot. −71.3° (26°, *c* 3, abs. $CHCl_3$, D line). Neither the α- nor the β-compound exhibited mutarotation in absolute or U. S. P. chloroform.

The α-isomer was soluble in chloroform and acetone, moderately soluble in hot ethanol and methanol, slightly soluble in ether and was practically insoluble in petroleum ether and water. The β-isomer was generally more soluble than its α-counterpart.

Anal. Calcd. for $C_5H_6O_5(CH_3CO)_5Br$; Br, 18.14; saponification value (6 equivs.), 13.60 c. 0.1 *N* NaOH per 100 mg. Found for α-isomer: Br, 18.21, saponification value, 13.73 cc. Found for β-isomer: Br, 18.05; saponification value, 13.66 cc.

α-1-Bromo-*aldehydo-d*-galactose Hexaacetate.—A solution of 10 g. of *aldehydo-d*-galactose pentaacetate[15] in 90 cc. of acetyl bromide was effected by heating just short of the boiling point for five minutes. The solution was treated with 4 cc. of the interconverting reagent under the same conditions as described previously and the product isolated in the same manner; yield 12 g. (91%), m. p. 125–135°, spec. rot. +52.5° (25°, *c* 2.9, abs. $CHCl_3$, D line).

The crude product was dissolved in hot acetone-petroleum ether and cooled to 5°. Three grams of crystalline material, m. p. 164–167°, spec. rot. −19.5° ($CHCl_3$), was separated by filtration and to the filtrate was added a large volume of petroleum ether. Upon cooling, the latter solution yielded 4.9 g. of a crystalline product; m. p. 139–141°, spec. rot. +90° ($CHCl_3$).

The levorotatory fraction was recrystallized twice from acetone–ether to yield 2 g. of β-1-bromo-*aldehydo-d*-galactose hexaacetate; m. p. 178–180°, spec. rot. −75° (25°, abs. $CHCl_3$, D line). Wolfrom[3] recorded as the constants of this compound: m. p. 179–181°, spec. rot. −79° (25°, abs. $CHCl_3$, D line). The dextrorotatory fraction was recrystallized thrice from acetone–petroleum ether and once from ether to yield 2 g. of pure α-1-bromo-*aldehydo-d*-galactose hexaacetate; m. p. 142.5–143°, spec. rot. +98.0° (17°, *c* 3, abs. $CHCl_3$, D line).

The α-modification crystallized from acetone-petroleum ether as elongated hexagonal plates. It was soluble in acetone and chloroform, moderately soluble in benzene, ethanol, and ether and was practically insoluble in petroleum ether and water. It was generally more soluble than its β-isomer.

Anal. Calcd. for $C_6H_7O_6(CH_3CO)_6Br$: Br, 15.57; saponification value (7 equivs.), 13.64 cc. 0.1 *N* NaOH per 100 mg. Found: Br, 15.64; saponification value, 13.70 cc.

Summary

1. α-1-Bromo-*aldehydo-d*-galactose hexaacetate and the α and β forms of the 1-chloro and of the 1-bromo derivatives of *aldehydo-d*-arabinose pentaacetate have been synthesized.

2. It is shown that the α and β forms of the 1-chloro and of the 1-bromo-*aldehydo-d*-galactose hexaacetate and the corresponding derivatives in the *d*-arabinose series, exhibit rotations that follow the isorotation rules of Hudson.

3. It is shown that the rotations of a number of other known acyclic α,β-forms of arabinose and mannose likewise follow the isorotation rules of Hudson quite closely.

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[15] M. L. Wolfrom. THIS JOURNAL, 52, 2464 (1930); M. L. Wolfrom and M. Konigsberg. *ibid.*, 61, 574 (1939).